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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/644,021 | 08/20/2003 | Ming-Hui Wei | CL001201DIV | 4849 |

25748 7590 02/08/2007

CELERA GENOMICS
ATTN: WAYNE MONTGOMERY, VICE PRES, INTEL PROPERTY
45 WEST GUDE DRIVE
C2-4#20
ROCKVILLE, MD 20850

| EXAMINER | |
|---|---|
| CROWDER, CHUN | |
| **ART UNIT** | **PAPER NUMBER** |
| 1644 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|---|---|---|
| 3 MONTHS | 02/08/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/644,021 | WEI ET AL. | |
| | Examiner | Art Unit | |
| | Chun Crowder | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07/21/2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *3,16,18,20,22 and 24-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3, 16, 18, 20, 22, 24-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures and the CRF Problem Report..

## DETAILED ACTION

1. Applicant's amendments, filed 07/21/2006, are acknowledged.

Claims 1-2, 4-15, 17, 19, 21, 23, and 27-29 have been canceled.
Claims 18 and 20 have been amended.

Claims 3, 16, 18, 20, 22, 24-26 are pending and currently under consideration as they read on the elected invention of an isolated antibody that selectively binds to polypeptide of SEQ ID NO:2 and a composition comprising the antibody

2. Applicant's submission of replacement sheets of figures which add sequence identifiers for sequences in Figure 2A, 2C, 2D and 3O-3Y is acknowledged and have been entered.

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures and the CRF Problem Report.

The computer readable form (CRF) diskette is damaged; also see CRF Problem Report mailed by STIC Biotechnology Systems Branch on 07/25/2006, which is attached herein.

Applicant is reminded of the Sequence Rules which require a submission for all sequences of 10 or more nucleotides or 4 or more amino acids (see 37 CFR 1.1821-1.1825) and is also requested to carefully review the submitted specification for any and all sequences which require compliance with the rules.

**Applicant must comply with the requirements of the Sequence Rules (37 CFR 1.1821-1.1825) in response to this Office Action.**

4. Applicant's submission of the new title of the invention is acknowledged and has been entered.

5. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter "pharmaceutically acceptable carrier" for reasons of record.

Applicant's arguments have been fully considered but have not been found persuasive.

Applicant argues that the phrase "pharmaceutically acceptable carrier" is in originally filed claim 10; as such the instant specification has written support for the phrase.

This is not found persuasive because the phrase "pharmaceutically acceptable carrier", even though is recited in originally filed claim 10, does not have written support in the specification as-filed.

Applicant is once again required to identify the written support for claims 22-25, particularly the claimed limitation of "pharmaceutically acceptable carrier".

Alternatively, applicant is invited to amend the specification to provide antecedent basis for the claimed subject matter.

6. Claims 3 and 16 stand rejected under **35 U.S.C. 102(b)** as being anticipated by Robinson (US Patent 5,589,372 cited in IDS filed 05/18/2005) as evidenced by Bost et al. (Immunol. Invest. 1988; 17:577-586) and Bendayan (J. Histochem. Cytochem. 1995; 43:881-886) for reasons of record.

Applicant's arguments have been fully considered but have not been found persuasive.

Applicant argues that in order for the teachings of Robinson to anticipated the instant claimed invention, the antibody taught by Robinson must necessarily selectively bind to instant polypeptide consisting SEQ ID NO:2, not possibly or probably bind the instant SEQ ID NO:2. Applicant further argues that antibody taught by Robinson does not necessarily selectively bind the instant polypeptide because the referenced squalene synthetase of SEQ ID NO:6 taught by Robinson is 98.4% homologous to the instant SEQ ID NO:2; as such the two polypeptides differ at least 1.6% in amino acid sequence which may encompass different epitopes. Thus, applicant concludes that due to the 1.6% amino acid sequence difference between the prior art SEQ ID NO:6 and the instant SEQ ID NO:2, the antibody taught by Robinson does not necessarily corss-react with the instant SEQ ID NO:2.

This is not found persuasive for following reasons:

Contrary to applicant's assertion that the prior art antibody does not necessarily cross-react with the instant SEQ ID NO:2, the examiner acknowledges that the prior art SEQ ID NO:6 is highly homologous to the instant SEQ ID NO:2 (98.4%), as such the prior art antibody to SEQ ID NO:6 would cross-react with the instant SEQ ID NO:2. There is strong evidence in the prior art that an antibody can be specific and cross-react with the antigen (Bost et al, Results, page 579 and Bendayan on page 886, last paragraph).

Applicant's attempt to limit an antibody that "selectively binds" to polypeptide consisting of SEQ ID NO:2 to exclude binding to other polypeptides (e.g. SEQ ID NO:6 of Robinson) that are highly homologous to the instant SEQ ID NO:2 is inconsistent with both the usage of the limitation in he instant specification and with the meaning ascribed to the phrase by one of ordinary skill in the art at the time the invention was made. For example, the instant specification on page 23 discloses that the claimed antibody is still considered to selectively bind a peptide even if it also binds to other proteins that are not substantially homologous with the target peptide so long as such proteins share homology with a fragment or domain of the peptide target of the antibody; it would be understood that antibody binding to the peptide is still selective despite some degree of cross-reactivity.

In this case, given that the claimed target peptide consisting of SEQ ID NO:2 is 98.4% homologous to the prior art SEQ ID NO:6 taught by Robinson, the prior art antibody to SEQ ID NO:6 would read on the claimed antibody, especially if antibody binding a peptide is still considered selective despite some degree of cross-reactivity (e.g. see page 23 of the instant specification).

Although the reference is silent about the antibody binding to the claimed SEQ ID NO: 2, it does not mean that the reference antibody does not bind this sequence, especially given the high homology shared between the prior art polypeptide and the instant polypeptide. Since the office does not have a laboratory to test the reference antibodies, it is applicant's burden to show that the reference antibodies do not bind to polypeptide consisting of amino acid sequence of SEQ ID NO:2 recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald* , 205 USPQ 594 (CCPA 1980); MPEP 2112.01.

The prima facie case that Robinson discloses the claimed antibody can be rebutted by evidence showing that the prior art product does not necessarily possess the characteristics fo the claimed product. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977). The arguments of counsel cannot take the place of objective evidence in the record. In re Schulze , 145 USPQ 716, 718 (CCPA 1965). See MPEP 716.01(c).

In that regard, applicant has not submitted any evidence showing that the Robinson antibody does not necessarily possess the characteristics of the claimed antibody.

Regarding applicant's assertion that distinct epitops might fall within the 1.6% different amino acid sequences between the prior art SEQ ID NO:6 and the instant SEQ ID NO:2, it is noted the instant invention does not identify any antigen epitops of the claimed SEQ ID NO:2, as such it's not clear what epitopes if any are in the 1.6% non-homologous regions.

Therefore the prior art antibody anticipates the claimed invention.

The rejection or record is maintained for the reasons of record. The rejection of record is incorporated by reference herein as if reiterated in full.

7. Claims 3, 16, 18, 20, 22, 24, and 25 are rejected under **35 U.S.C. 103(a)** as being unpatentable over Robinson (US Patent 5,589,372 cited in IDS filed 05/18/2005) in view of Bost et al. (Immunol. Invest. 1988; 17:577-586), Bendayan (J. Histochem. Cytochem. 1995; 43:881-886), and Harlow et al. (Antibodies, A Laboratory Manual 1988, pages 319-358) for reasons of record.

Applicant's arguments have been fully considered but have not been found persuasive.

Applicant's arguments and the examiner's rebuttal regarding the teachings of Robinson are essentially the same as discussed above in Section 6.

Applicant further asserts that Harlow et al. even in combination with Robinson, Bost et al. and Bendayan does not make obvious the instant claimed antibody because SEQ ID NO:6 taught in Robinson differs at least 1.6% in amino acid sequence from the instant SEQ ID NO:2.

This is not found persuasive for reasons of record and the discussion above in Section 6 regarding the teachings of Robinson.

Further, given the teachings of Robinson, Bost et al. and Bendayan regarding the antibody specific for squalene sythetase that shares 98.4% homology with the claimed polypeptide comprising SEQ ID NO:2, and the teachings Harlow et al, regarding that coupling antibodies directly to a detectable substance provide fewer steps and less background in immunoassay, the ordinary artisan at the time the invention was made would have had a reasonable expectation success to produce antibody that binds to polypeptide of SEQ ID NO:2 coupled to a detectable substance in carriers such as PBS.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

The rejection or record is maintained for the reasons of record, as it applies to the amended claims. The rejection of record is incorporated by reference herein as if reiterated in full.

8. Claim 26 stands rejected under **35 U.S.C. 103(a)** as being unpatentable over Pluckthun et al. (Immunotechnology 1997, 3:83-105) in view of Robinson (US Patent 5,589,372 cited in IDS filed 05/18/2005), Bost et al. (Immunol. Invest. 1988; 17:577-586), and Bendayan (J. Histochem. Cytochem. 1995; 43:881-886) for reasons of record.

Applicant's arguments have been fully considered but have not been found persuasive.

Applicant's arguments and the examiner's rebuttal regarding the teachings of Robinson are essentially the same as discussed above in Section 6.

Applicant further asserts that Pluckthun et al. even in combination with Robinson, Bost et al. and Bendayan does not make obvious the instant claimed antibody because SEQ ID NO:6 taught in Robinson differs at least 1.6% in amino acid sequence from the instant SEQ ID NO:2.

This is not found persuasive for reasons of record and the discussion above in Section 6 regarding the teachings of Robinson.

Here, given the teachings of Pluckthun et al. regarding the antibody fragments, and the teachings of Robinson, Bost et al, and Bendayan providing method and the use of antibodies that bind polypeptide of SEQ ID:2, the ordinary artisan at the time the invention was made would have had a reasonable expectation of success producing antibody fragments such as Fab, $F(ab')_2$, and Fv that binds polypeptide of SEQ ID NO:2.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

The rejection or record is maintained for the reasons of record. The rejection of record is incorporated by reference herein as if reiterated in full.

9. Upon further consideration as well as applicant's amendment, the previous rejections under 35 U.S.C. 112, first and second paragraphs have been withdrawn.

10. Conclusion: no claim is allowed.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Crowder whose telephone number is (571) 272-8142. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chun Crowder, Ph.D.
Patent Examiner
February 1, 2007

PHILLIP CAMBEL, PH.D
PRIMARY EXAMINER
TC 1600
2/5/07

Application No.: 10/644,021

# NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☒ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other: _____

## Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

**PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE**

10/644,021

## STIC Biotechnology Systems Branch

1FW16

## CRF Problem Report

**The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) experienced a problem when processing the following computer readable form (CRF):**

Application Serial Number: 10/644,021B
Filing Date: 8/20/03
Date Processed by STIC: 7/25/06

STIC Contact: **Mark Spencer: Telephone: 571-272-2510; Fax: 571-273-0221**

**Nature of CRF Problem:**

____ (circle one) Damaged or Unreadable (for Unreadable, see attached)
____ Blank (no files on CRF) (see attached)
____ Empty file (filename present, but no bytes in file) (see attached)
____ Wrong file saved to CRF (invention title, docket number, or applicant(s) do not match those in official application) (see attached)
____ Not saved in ASCII text
____ Sequence Listing was embedded in the file. According to Sequence Rules, submitted file should **only** be the Sequence Listing.
____ Did not contain a Sequence Listing. (see attached sample)
__J__ Other: bad disk sector (see attached)

**PLEASE USE THE CHECKER VERSION 4.4.0 PROGRAM TO REDUCE ERRORS. SEE BELOW FOR ADDRESS:**
**http:/www.uspto.gov/web/offices/pac/checker/chkrnote.htm**

1. EFS-Bio (<http://www.uspto.gov/ebc/efs/downloads/documents.htm>, **EFS Submission User Manual** - ePAVE)
2. **U.S. Postal Service:** Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
3. **Hand Carry, Federal Express, United Parcel Service, or other delivery service (EFFECTIVE 01/14/05):** U.S. Patent and Trademark Office, Mail Stop Sequence, Customer Window, Randolph Building, 401 Dulany Street, Alexandria, VA 22314

Revised 01/20/06

10/6440218

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A:\>

Onscreen messages at this portion of submitted diskette. This could be due to a bad disk sector.